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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

PAK, YONG D

ART UNIT PAPER NUMBER

1652

DATE MAILED: 08/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/090,965

Applicant(s)

SRIENC ET AL.

Examiner

Yong D. Pak

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 June 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

The after final response filed on June 24, 2005 has been entered.

Claims 1-13 are pending and are under consideration.

Response to Arguments

Applicant's amendment and arguments filed on June 24, 2005, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Finality of the rejection of the last Office is withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-13 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Madison et al., Johnston et al., Clemente et al., and Linde et al.

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Claims 1-13 are drawn to a method of producing PHA in *S. cerevisiae* or *Kluyveromyces* by introducing polynucleotide encoding a PHA_{SCL} or PHA_{MCL} and a polynucleotide encoding an acetoacetyl-CoA reductase and/or a β -ketothiolase.

Madison et al. teach a method of producing PHA in *S. cerevisiae* by introducing DNA encoding an *A. eutrophus* PHA polymerase (page 44). Madison et al. teach that low levels of PHA was due to insufficient activity of the endogenous β -ketothiolase and acetoacetyl-CoA reductase and points to improving PHA yields in *S. cerevisiae* by increasing the activities of these two enzymes.

Further, Madison et al. teach other PHA_{SCL} and PHA_{MCL} that can be used in transgenic yeasts (pages 24-35) and that many different transgenic organisms can be used to produce PHA (page 44), such as a *Kluyveromyces*, which also belongs to the family of *Saccharomycetaceae* like *S. cerevisiae*.

The difference between the reference of Madison et al. and the instant invention is that the reference of Madison et al. does not teach a method of producing PHA anaerobically using a yeast transformed a single nucleic construct comprising at least two of β -ketothiolase, acetoacetyl CoA reductase or PHA_{SCL} or PHA_{MCL}.

However, expression of multiple heterologous genes in yeast is routine in the art. Also, making a single nucleic acid construct composed of more than one or two genes is also very routine in the art (Strategene catalog, cited in previous Office Action). For example, Clemente et al. (U.S. Patent No. 5,489,894 – form PTO-892) discloses a method of expressing three genes via a single nucleic acid construct (Columns 15-16).

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Johnston et al. discloses using divergent promoters to express more than one gene in *S. cerevisiae*.

Regarding the limitation of producing PHA under anaerobic conditions, it is well known in the art that *S. cerevisiae* is able to grow both aerobically and anaerobically (Visser et al., Ohmori et al., Linde et al., Nissen et al.). It is also well known in the art that oxygen can cause serious stress to living organisms, including yeasts (Linde et al. and Nissen et al.). Linde et al. also discloses that gene expression under anaerobic and anaerobic culture conditions showed little difference (page 7412). From the teachings in the art and Linde et al., one having ordinary skill in the art would have recognized to use transgenic *S. cerevisiae* and *Kluyveromyces*, under anaerobic or aerobic conditions, permitting flexibility in culture conditions and thereby improving cost effectiveness of producing PHA.

Therefore, with the references of Madison et al., Johnston et al., Clemente et al., and Linde et al. in hand, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make a transgenic *S. cerevisiae* or *Kluyveromyces* yeast comprising the heterologous PHA polymerase, β -ketothiolase and/or acetoacetyl CoA- reductase. The motivation of further expressing said enzymes via a single nucleic acid construct is to control and increase activity of said enzymes to increase the yield of PHA. The motivation of producing polyhydroxyalkanoates under anaerobic conditions would be to increase efficiency of the production of polyhydroxyalkanoates. One of ordinary skill in the art would have had a reasonable expectation of success since Madison et al. teach that an increase in activity of β -

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ketothiolase and an acetoacetyl CoA- reductase in yeast transformed with PHA_{SC}L or PHA_{MCL} will increase the yield of PHA, Clemente et al. and Johnston et al. both teach expression of multiple genes, and Linde et al. teaches flexibility of expressing genes in anaerobic and aerobic culture conditions, thereby improving cost effectiveness of producing PHA.

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that Madison et al. do not teach anaerobic culture conditions. In order to address that argument, Examiner has issued a new rejection citing new art.

Applicants argue that the teachings of the secondary references do not teach production of PHA in yeast. While Clement et al. disclose using bacteria, the reference of Clement et al. is relied upon only to demonstrate that constructing a single polynucleotide comprising several genes was known in the art. The new rejection above cites Johnston et al., which teaches expression of multiple genes in yeast.

Applicants argue that transgenic bacterial cells were restricted from transgenic yeast cells and therefore, they are patentable over each other. Examiner respectfully disagrees. Since Madison et al. discloses a method of producing PHAs using transgenic yeasts and the rejection cites new references from which it would have been obvious to one having ordinary skill in the art to culture transgenic yeasts under anaerobic condition.

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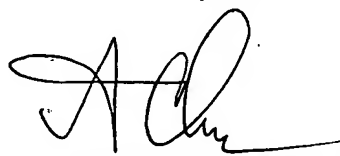
None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak
Patent Examiner 1652



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